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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/767,412	JOHNSTON ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-63* is/are pending in the application.

4a) Of the above claim(s) *42,46 and 61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *41,43-45,47-60,62 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/26/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (Claims 41-63 in part) in the reply filed on 9/12/2005 is acknowledged. The traversal is on the ground(s) that the antigen is administered using the same steps/or reagents as the administration of the nucleic acid. This is found persuasive. It has been noted according to the specification disclosure that claimed antigen is a product expressed by the claimed nucleic acid (or expression vector) administered to an animal. That is the claimed nucleic acid is administered to an animal, and the encoded protein (antigen) will be expressed within that animal and therefore elicit an immune response. Thus, restriction between nucleic acid (Group I) and the encoded antigen (Group II) are withdrawn.

2. Applicant's election with traverse of the following species in the reply filed on 9/12/2005 is acknowledged. Applicant elected CMV as a promoter and hGh as the signal sequence. The traversal is on the ground that the no specific species was claimed, and therefore species election is not proper. This is not found persuasive since species elections are deemed proper if the claims are drawn to a genus.

3. Applicant's election **without** traverse of the following species in the reply filed on 9/12/2005 is acknowledged. Applicants elected: A: mouse; B: human; C: bacterial cell; D: E.coli; E: human growth hormone; H: about 400bp.

4. Claims 42, 46 and 61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species, there being no allowable generic or linking

claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/12/2005.

5. Claims 41-63 are currently pending;

Claims 42, 46 and 61 have been withdrawn;

Claims 41, 43-45, 47-60, 62 and 63 are being examined in this application.

Priority

6. This application is a continuation of U.S. Application Ser. No. 09/448,330, filed November 22, 1999 (abandoned on 3/26/2004); which application is a divisional of U.S. Application Ser. No. 09/001,157, filed December 30, 1997, now issued as U.S. Patent No. 5,989,553; which application is a divisional of U.S. Application Ser. No. 08/421,155, filed April 7, 1995, now issued as U.S. Patent No. 5,703,057.

Specification

7. The disclosure is objected to because of the following informalities:

A.) No brief description for each one of the Figure 1A, 1B, 1C, and 1D.

B.) The filing date for the US Application No. 09/001,157 should be 12/20/1997 on Page 2, line 2 of the specification. (See Specification Amendment filed on 1/29/2004.)

Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 41, 43-45, 47-60, 62 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims recite a method comprising obtaining a nucleic acid encoding an antigen or an antigen encoded by the nucleic acid; selecting a nucleic acid; and administering the nucleic acid or antigen to a subject. In Claim 1, the claimed method used for the recited method is not clearly defined. One would interpret the Claim to read that both the nucleic acid and/or antigen are administered to a subject. One would also interpret the Claim to read that the nucleic acid administered to a subject would elicit the wanted immune response without the expression of the antigen. DNA vaccination and antigen vaccination are different from each other and involves different molecular interaction, where one (DNA) involves DNA-protein interaction, and the other (protein antigen) involves protein-protein interaction. In addition, the administering procedure for vaccination with DNA and antigen (protein) would be different as well. For example, protein antigen could be produced by other host cells and then administered directly to a subject without the nucleic acid. Furthermore, identification of nucleic acid would differ from the techniques for identifying the protein antigen. Therefore, the instant claims fail to particularly point and distinct claim the subject matter.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

10. Claims 41, 43-45, 47-60, 62 and 63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims briefly recite a method comprising obtaining a nucleic acid encoding an antigen comprising the following steps: obtaining a library comprising DNA sequences from a pathogen; introducing a plurality of members of said library into an animal; and selecting and identifying the nucleic acid from the library that elicit an immune response. The method is further comprised of administering the nucleic acid to a subject.

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

Written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not case involves question of priority, since requirement applies to all inventions including chemical inventions, and since the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not

remove patentee's obligation to provide description of compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

Although the instant specification recites examples of expression library generated by using genomic DNA from a bacteria (Mycoplasma pulmonis) and administering in an animal/subject (mouse), the instant specification and/or the aforementioned claims do not provide adequate written description to show possession of the entire genus of using the method with any pathogens and/or animals. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only detailed description is the generation of one particular bacterial gene library and injection into one species of an animal. Procedures of isolation and genomic fragmentation of other species of pathogen might be dramatically different from the claimed method. In addition, injection of genetic material in different animals such as human might entail different techniques and dosages.

As discussed above, the skilled artisan cannot envision the detailed procedures for utilizing the method in the encompassed genus of "pathogens" and "animal/subject," and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of creating such composition. Adequate written description requires more than a mere statement that it is part of the invention and reference to a possibility of creating it.

Therefore, the instant Claims 41, 43-45, 47, 48, 50-60, 62 and 63 do not meet the written description provision of 35 U.S.C. 112, first paragraph.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 50, and 54-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant claims, the word "about" is indefinite since the terminology does not appear to have been defined in the specification as to clearly state the specific range that the recited number can vary. Therefore, no clear defined metes and bounds for the claimed subject matter are provided.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 41, 43, 48, 50-60 and 62 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 52-65 of copending Application No. 10/023,437. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference patent application recites the essential steps and products claimed in the instant application. For example, Claims 52-65 recite a method of preparing and administering polynucleotide sequences (library) to an animal (vertebrate animals), and subsequent selecting and identifying a polynucleotide (and/or antigen). Therefore, it would have been obvious for one of ordinary skilled in the art to modify the reference claimed method to vaccinate a subject with nucleic acids derived from any pathogen (especially bacterial) genome library as taught by the reference.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 41, 43, 44, 48-52, 54-60 and 62 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 and 27-30 of U.S. Patent No. 5,703,057 (henceforward refers to as '057 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '057 patent claims the same method of screening for an antigen (and or polynucleotide expression vector) and elicit an immune response in an animal. For example, Claims 1-19 of the '057 patent recites a method comprising preparing a set of cloned expression libraries; and generating an immune response by introducing a plurality of clones into an animal. Further more, Claim 6 of the reference, for example, recites identifying the antigens that were responsible for eliciting the immune response.

Therefore, it would have been obvious for one of ordinary skilled in the art to modify the reference claimed method to vaccinate a subject with nucleic acids derived from a bacterial genome as taught by the reference.

16. Claims 41, 43, 59-60, 62 and 63 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,410,241 B1 (henceforward refers to as '241 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '241 patent claims the same method of screening for an antigen (and or polynucleotide expression vector) and elicit an immune response in an animal. For example, Claim 1 of the '241 patent recites a method of preparing at least one element (read on a library) comprising an open reading frame linked to a promoter, and generate an immune response by introducing the elements into an animal. Further more, Claim 16 of the reference, for example, recites identifying the antigens that were responsible for eliciting the immune response. Therefore, it would have been obvious for one of ordinary skilled in the art to modify the reference claimed method to vaccinate a subject with nucleic acids derived from any pathogen (especially bacterial) open reading frame library as taught by the reference.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 41, 43-45, 47-50, 54-56, 59 and 62 are rejected under **35 U.S.C. 102(b)** as being anticipated by Lai et al (Vaccine. Vol 12: 291-298; March, 1994).

The instant claims briefly recite a method comprising obtaining a nucleic acid encoding an antigen comprising the following steps: obtaining a library comprising DNA sequences from a pathogen; introducing a plurality of members of said library into an animal; and selecting and identifying the nucleic acid from the library that elicit an immune response. The method is further comprised of administering the nucleic acid to a subject.

Lai et al teach screening a library of DNA constructs derived from *Mycoplasma pulmonis* (MP; a bacterial pathogen), and immunizing animals with selected constructs against MP (See Abstract). The reference teaches the construction of library by using sheared MP DNA fragments of 200-500 bp (page 292, left column, last paragraph). The reference further teaches *E. Coli* (bacterial cells) is used as host for preparing the library (See Materials and Methods section). The reference also teaches the size of the generated library in term of 1.6X10^5 p.f.u/2ug of DNA (page 294, left column, 3rd paragraph). In addition, the reference teaches injecting bacterial suspension (containing plurality of plasmid constructs) into mice (Page 293, 2nd paragraph), and would refer to administer the nucleic acid to a subject. The reference also teaches selecting four clones (page 293, 1st paragraph), and sequencing analysis to identify the insert in the plasmid construct (Page 295). This would refer to selecting and identifying the nucleic acid.

Thus, the reference clearly anticipates the claimed invention.

19. Claims 41, 45, 47, 48, 59, 60 and 62 are rejected under **35 U.S.C. 102(a)** as being anticipated by Coney et al (Vaccine. Vol 12: 1545-1550. 12/1994).

The instant claims briefly recite a method comprising obtaining a nucleic acid encoding an antigen comprising the following steps: obtaining a library comprising DNA sequences from a pathogen; introducing a plurality of members of said library into an animal; and selecting and identifying the nucleic acid from the library that elicit an immune response. The method is further comprised of administering the nucleic acid to a subject.

Coney et al teach administering DNA to rodents and non-human primates to elicit immune responses against expressed HIV antigens. The reference teaches the production of several DNA constructs encoding various HIV proteins (page 1546, right column, 3rd paragraph). This would refer to "obtaining a library comprising DNA or RNA sequence from a pathogen." The reference also teaches administering the constructs (for example, constructs pM160-HXB2 and pM160-Z6 were administered separately or together) (Page 1547, left column, paragraph 2), which would read on "introducing a plurality of members of said library into an animal, and selecting at least a first member form the library that elicits an immune response to identify said nucleic acid or antigen." The reference further teaches inoculating cynomologous monkeys with pM160-Z6 construct and analyzing the monkeys' immune responses (Page 1548, right column, 1st paragraph). This would read on "administering the nucleic acid...to a subject..." of the instant claim. In addition, the reference teaches the inoculated DNA are plasmid constructs (page 1546, right column, 3rd paragraph), which are cloned and would have been prepared using

bacterial host cells. The reference further teaches the DNA constructs were analyzed by restriction (page 1546, right column, 3rd paragraph). The reference also teaches the DNA constructs were injected into the animals (page 1546, right column, 4th paragraph).

Thus, the reference clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 41, 43-45, 47-60, 62 and 63 are rejected under 35 U.S.C. 103(a) as being obvious over Lai et al (Vaccine. Vol 12: 291-298; March, 1994), in view of Felgner et al (US Patent No. 5,589,466).

The instant claims briefly recite a method comprising obtaining a nucleic acid encoding an antigen comprising the following steps: obtaining a library comprising DNA sequences from a pathogen; introducing a plurality of members of said library into an animal; and selecting and identifying the nucleic acid from the library that elicit an immune response. The method is further comprised of administering the nucleic acid to a subject.

Lai et al teaches screening a library of DNA constructs derived from *Mycoplasma pulmonis* (MP; a bacterial pathogen), and immunizing animals with selected constructs against MP as aforementioned.

Lai et al do not teach the DNA sequences of a pathogen is fused to a mammalian fusion gene (such as human growth hormone), and the expression construct contains a promoter. The reference also does not teach the range and/or specific amount of DNA that is injected into an animal. In addition, the reference also does not teach the DNA is chemically synthesized.

However, Felgner et al teach injecting human growth hormone fusion protein expression constructs into a mammal (a human). (See Example 18 and Claim 5) The reference further teaches the expression construct comprises a promoter sequence which can control the expression of the DNA in mammal. Furthermore, the reference teaches the benefit of polynucleotide encoding for a secretable therapeutic polypeptide (such as growth hormone) that is it can be released into the circulation to seek a metabolic target (Column 14, lines 5-15). The reference also teaches the general range of DNA to be injected into an animal (about 0.05 ug/kg to about 50 mg/kg), which will vary depending on the activity of the particular peptide. (Column 15, lines 40-53) The reference also teaches the DNA inserts can be synthesized directly due to the availability of automated nucleic acid synthesis equipment (Column 11, lines 15-21).

Therefore, it would have been prima facie obvious for an ordinary skilled artisan to screen for polypeptides encoded by polynucleotides that can be used to vaccinate a subject. Due to the advantages taught by Felgner et al, a person of ordinary skill in the art would have been motivated at the time of the invention to modify the expression constructs taught by Lai et al to include a gene for a fusion mammalian protein (human growth hormone) and a mammalian expression promoter region, and to adjust the injection dosage according to the activity of the antigen. An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications since the techniques for chemically synthesizing DNA fragments, cloning

mammalian expression vectors, and constructing fusion genes are known and routine in the art as taught by Lai et al and Felgner et al.

In conclusion, the invention of the instant claims would have been prima facie obvious over Lai et al, in view of Felgner et al to one of ordinary skill in the art without evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PADMASHRI PONNALURI
PRIMARY EXAMINER

SL
Art Unit 1639
10/21/2005